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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/738,540	12/14/2000	Wyne Pun Lee	P1795R1	2012
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9157	7590	09/12/2003
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GENENTECH, INC.
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EXAMINER

HADDAD, MAHER M

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 09/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/738,540	LEE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6 and 18-25 is/are pending in the application.
- 4a) Of the above claim(s) 21-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6, 18 -20 and 24-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

1. Applicant's amendment, filed 8/13/03, is acknowledged.
2. Claims 1,6 and 18-25 are pending.
3. Claims 21-23 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
4. Claims 1, 6, 18-20 and 24-25 are under consideration in the instant application as they read on a method of treating rheumatoid arthritis, comprising administering to mammal in need thereof effective amounts of an anti-CD11a antibody and a TNF- α antagonist wherein the TNF- α antagonist is TNF- α receptor-IgG Fc fusion protein.
5. Applicant's statement that both '454 and the present application were assigned to Genentech, Inc. and were commonly owned at the time the claimed invention was made is sufficient to overcome the previous rejection under 103(a).
6. The Finality of the previous Office action is hereby withdrawn in view of the new grounds of rejections.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 6, 18-19 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,690,933, in view of U.S. Patent No. 6,306,820 (of Record) as is evidenced by the known fact disclosed in the specification on page 16, line 5 and page 17, lines 4-5.

The '933 patent teaches the use of a CD11a mAb, a non-depleting mAb, in conjunction with other immunosuppressive agents, to treat autoimmune diseases such as rheumatoid arthritis (see col., 3, lines 11-55 and patented claims 1-4 in particular).

Art Unit: 1644

The claimed invention differs from the reference teachings only by the recitation of TNF- α antagonist, wherein the TNF- α antagonist is a TNF- α receptor IgG fusion protein in claim 1, the fusion protein consists of the extracellular ligand binding portion of human tumor necrosis factor receptor linked to the hinge region, CH2 domain, and CH3 domain of human IgG1 in claim 18 and the method of treating an LFA-1 or a TNF- α mediated disorder, further comprising administering to the mammal an effective amount of methotrexate in claim 19.

The '820 patent teaches the ability of TNFbp product(s) (e.g., sTNFR-I, sTNFR-II, sTNFR fragments (2.6 D sTNFRs such as 2.6 D sTNFR-I) or sTNFR Fc(s) (sTNFR-I/IgG1 or sTNFR-II/IgG1) and methotrexate to act synergistically in the treatment of various symptoms associated with TNF-mediated diseases, including acute and chronic inflammation such as rheumatic diseases. The '820 patent further teaches the amino-terminal or carboxy-terminal fusion of a TNFbp(s) with all or part of the constant domain of the heavy or light chain of human immunoglobulin (individually or collectively, ("sTNFR Fc(s)"). Such chimeric polypeptides are preferred wherein the immunoglobulin portion of each comprises all of the domains except the first domain of the constant region of the heavy chain of human immunoglobulin such as IgG (e.g., IgG1 or IgG3) (column 6, lines 56-65 in particular). Finally, the '820 patent teaches that the combined treatment with TNFbp product(s) and methotrexate has the advantage of achieving the same result with a lower dose or less frequent administration of methotrexate, thereby reducing any toxic effect (column 35, lines 47-67 and column 36, line 1-2 in particular).

As is evidenced in the specification on page 17, lines 4-5, that the claimed TNF- α antagonist is a TNF- α receptor-IgG Fc fusion protein, such as ENBREX (Immunex) is known. ENBREX consists of the extracellular ligand-binding portion of the tumor necrosis factor receptor (TNFR) linked to the Fc portion of human IgG1. The Fc component of ENBREX contains the CH2 domain, the CH3 domain and hinge region (page 3, lines 6-9 in particular).

Claim 24 is included because it would be conventional and within the skill of the art to identify and determine the optimum administration protocol of the anti-CD11a antibody and the fusion protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the well known ENBREX as is evidenced in the specification on page 17, lines 4-5, or TNF- α receptor-IgG Fc fusion protein in combination with methotrexate taught by the '820 patent with the immunosuppressive agent taught by the '933 patent in a method of treating rheumatoid arthritis.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because immunoadhesin exploit both the natural affinity of a receptor for its ligand and the effector functions of the immunoglobulin Fc region. Also, the combined treatment with sTNFR Fc(s) and methotrexate has the advantage of achieving the same result with a lower dose or less

Art Unit: 1644

frequent administration of methotrexate, thereby reducing any toxic effect taught by the '820 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,690,933, in view of U.S. Patent No. 6,306,820 (of Record) as is evidenced by the known fact disclosed in the specification on page 16, line 5 and page 17, lines 4-5 as applied to claims 1, 6, 18-19 and 24-25 above, and further in view of Owens *et al* (1994).

The teachings of '933 and '820 patents and the evidentiary disclosure have been discussed, *supra*.

The claimed invention differs from the reference teaching only by the recitation of a humanized antibody in claim 20.

Owens *et al* teach the modification of murine antibodies such as a humanized antibody. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. (see the entire document).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the monoclonal antibody taught by '933 patent as humanized antibody taught by the Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.


8. No claim is allowed.

Art Unit: 1644

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
September 10, 2003


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